UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/507,242	02/18/00	HANES S	454311-2200.

020999
FROMMER LAWRENCE & HAUG
745 FIFTH AVENUE
NEW YORK NY 10151

HM22/0618

EXAMINER
BASKAR, P

ART UNIT	PAPER NUMBER
1645	6

DATE MAILED: 06/18/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File Copy.

Office Action Summary	Application No.	Applicant(s)	
	09/507,247	~~FREDRECKSEN ET AL.~~ Hanas et al	
	Examiner	Art Unit	
	Padmavathi v Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *3,4 and 7-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,5,6 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims *1-23* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

1. In order to expedite the correlation of papers with the application please direct all future correspondence to Technology Center 1600, Art Unit 1645.

Priority

2. Applicant's domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application 60/121,246 is not available to the Examiner at present. Therefore, priority will be granted after reviewing the provisional application 60/121,246.

Drawings

3. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See PTO-948 for details. Correction of the noted defects can be deferred until the application is allowed by the examiner.

Election/Restriction

4. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I Claims 1 - 2, 5, 6 and 20 - 23, drawn to DNA, associated primers and vector and a method of making CaEss1 classified in class 536, subclass 23.5.

II. Claims 3-4, drawn to proteins, classified in class 530, subclass 350.

III. Claim 7 drawn to a method for detecting C.albicans comprising a nucleic acid molecule, classified in class 435, subclass 6.

IV. Claim 8 drawn to a method for detecting C.albicans comprising a detecting the presence of polypeptide, classified in class 435, subclass 7.1

V Claim 9, drawn to an antibody, classified in class 530, subclass 387.1.

VI Claim 10, drawn to a diagnostic composition comprising the polypeptide, classified in class 424, subclass 184.1.

VII Claim 11-13, drawn to a diagnostic composition comprising nucleic acid molecule class 536, subclass 23.1.

VIII Claims 14, 15, 16 and 18, drawn to a compound and a method for preventing or treating C.albicans, classified in class 424, subclass 130.1.

IX. Claims 17 and 19 drawn to an antiproliferative compound and a method for preventing human cell growth classified in class 424, subclass 1.41

5. The inventions are distinct, each from the other because of the following reasons: Invention I drawn to a DNA molecule, and Invention II drawn to a protein. These inventions are drawn to different products and are distinct from method Groups, III, IV, VIII and IX since they are products with different structure and biological properties. The protein is made of amino acids whereas the nucleic acid molecule consists of nucleotides. Further methods (Groups, III, IV, VIII and IX) known in the art used to detect or prevent the C.albicans and prevent cell growth does not require the nucleic acid or protein or antibody. For instance, C.albicans can be detected by culturing the microorgansim or by microscopic examination, the disease can be treated or prevented with anti-fungal drugs such as fluconazole and cell growth can be prevented by radiation treatment.

Invention V drawn to an antibody is distinct from Inventions I-II, VI and VII since it has an inherent affinity, avidity, and specificity that DNA or a simple protein is not capable of expressing.

Invention VI, drawn to a diagnostic composition and is distinct from Inventions I-II, V, and VII since it has a distinct primary amino acid sequence, radio labels, enzymes and compounds which imparts unique biological structure and functions.

Inventions VII drawn to a diagnostic composition and is distinct from Inventions I-II, V and VI, since it has a distinct primary nucleic acid sequence, radio labels, enzymes and compounds which imparts unique biological structure and functions and has added biological function of interacting with the nucleic acids

Inventions III, IV, VIII and IX drawn to patentably distinct methods of detecting, preventing/treating C.albicans and method of preventing human cell growth respectively, are distinct from the Inventions of Groups I, II, V, VI and VII since they require additional biological reagents and parameters for detecting, preventing/treating C.albicans or preventing cell growth. All these methods (Inventions III, IV, VIII and IX) are different to each other in utilizing different reagents, different method steps and the final outcome is different.

6. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their separate classification and their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

7. During a telephone conversation with Thomas Kowalski on 5/1/01 a provisional election was made with traverse to prosecute the invention of I, claims 1, 2, 5, 6 and 20 - 23. Affirmation of this election must be made by applicant in replying to this Office action. Claims 3-4 and 7-19 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the

application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(l).

Claim Rejections - 35 USC 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1and 2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant specification does not contain a written description of the invention for a nucleotide sequence which has at least 70% homologyl to the nucleotide sequence of SEQ.ID.NO 1 in such full, clear, concise, and exact terms or in sufficient detail that one skilled in the art can reasonably conclude that applicant had possession of the claimed invention at the time of filing.

The claims are drawn to isolated DNA molecules

a) comprising SEQ.ID.No1 and a sequence comprising at least 70% identity to SEQ ID NO: 1

b) comprising a nucleic acid encoding CaESS1 at least 70% identity to SEQ ID NO: 1

The claims are further drawn to vectors comprising the above sequences and host cells transfected with them.

The specification discloses an isolated cDNA sequence, SEQ ID NO: 1, which encodes a predictive polypeptide sequence, SEQ ID NO. 2. Absent evidence to the contrary, each of the SEQ ID NOS elected for examination is deemed to be an incomplete cDNA (i.e., cDNA with 70% identity to SEQ ID NO: 1). Because the cDNA that corresponds with 70% identity to SEQ ID NO: 1 mentioned in the claim is not a full-length, a sequence prepared from undefined parts of a cDNA clone will not comprise the entire coding region of any particular gene, nor is it clear the partial sequence is even in frame to encode a polypeptide. The claim, as written, however, encompasses polynucleotide, which vary substantially in length and also in nucleotide composition. The broadly claimed genus additionally, encompasses Candida albicans genes, as well as genes incorporating only portions of the disclosed sequence.

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly & Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotide. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings

sufficient to enable one of skill to isolate and identify the polynucleotide encompassed and no identifying characteristic or property of the instant polynucleotide is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

The specification further fails to identify and describe the 5' and 3' regulatory regions and untranslated regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the gene. The art indicates that the structures of genes with naturally occurring regulatory elements and untranslated regions is empirically determined (Ahn et al. Nature Genetics 3(4): 283-91, 1993 and Cawthon et al. Genomics 9(3): 446-60, 1991). Therefore, the structure of these elements is not conventional in the art and one skilled in the art would therefore not recognize from the disclosure that applicant was in possession of a nucleotide sequence which is at least 70% identical to the nucleotide sequence of SEQ.ID.NO 1. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

11. Claims 1, 2, 5 and 20-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated or purified nucleic acid consisting of SEQ. ID. NOS: 1, primer or probe consisting of OW-216 or OW-221 (SEQ.ID.NOS 3 or 6), a method for obtaining an isolated nucleic acid molecule encoding CaESS1 consisting of performing a polymerase chain reaction on a sample to contain CaESS1 using a primer or probe consisting of OW-216 or OW-221 (SEQ.ID.NOS 3 or 6) which specifically hybridize thereto, does not reasonably provide enablement for a nucleic acid molecule comprising a nucleotide sequence encoding any and all variants of CaESS1, (i.e., variant with 70%homology) any primer or probe which specifically binds to a nucleic acid molecule comprising a nucleotide sequence encoding

any and all variants of CaESS1,and a method for obtaining any and all variants of isolated nucleic acid molecule encoding CaESS1 comprising performing a polymerase chain reaction on a sample to contain variants of CaESS1 using any primer or probe which specifically hybridizes thereto . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant specification provides insufficient support for said recitation. Applicants have provided insufficient guidance exactly where to find support in the originally filed specification for the claimed invention as set forth above. Examiner has reviewed the specification and found no support for such language. The specification recites (pages 37-38 and example 3) nucleic acid molecule SEQ.ID.NO 1 and the deduced amino acid sequence SEQ.ID.NO 2, primer or probe consisting of OW-216 or OW-221 (SEQ.ID.NOS 3 or 6), a method for obtaining an isolated nucleic acid molecule encoding CaESS1 consisting of performing a polymerase chain reaction on a sample to contain CaESS1 using a primer or probe consisting of OW-216 or OW-221 (SEQ.ID.NOS 3 or 6). However, there is no support for a nucleic acid molecule which encodes a fragment of a polypeptide (i.e., fragment with 70% homology) and a primer or probe which specifically binds to a nucleic acid molecule comprising a nucleotide sequence encoding any and all variants of CaESS1,and a method for obtaining an isolated nucleic acid molecule encoding CaESS1 comprising performing a polymerase chain reaction on a sample to contain CaESS1 using any primer or probe which specifically hybridize thereto Therefore, applicant is advised to point to the specification where support for this claimed language is found and how it conveys the concept of the instant claims .

Scope of enablement requires that the specification teach those in the art to make and use the invention commensurate with the scope of the claim without undue experimentation

include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

Applicant has not set forth which nucleic acid molecule encodes a fragment with 70% homology, any probe or primer which hybridizes to the nucleic acid molecule of SEQ.ID.NO 1 and a method for obtaining an isolated nucleic acid molecule encoding a variant of CaESS1 comprising performing a polymerase chain reaction on a sample to contain CaEss1 using any primer or probe. Neither the fragments nor the variants as presently claimed is set forth clearly in the specification.

The instant claims comprising nucleic acid molecule encoding a fragment with 70% homology, any probe or primer which hybridizes to the nucleic acid molecule of SEQ.ID.NO 1 and a method for obtaining an isolated nucleic acid molecule encoding a fragment with 70% CaESS1 comprising performing a polymerase chain reaction on a sample to contain CaEss1 using any primer or probe are not predicted. The specification provides guidance and direction with regard to SEQ.ID.NO 1. 3 and 6 However, there is no guidance or directions on how to make and how to use a polypeptide comprising fragments or variants of CaEss1 with a deletion, of one or more amino acid residues in the amino acid sequence and still retain activity and the ability to generate antibodies. Undue experimentation, without a reasonable expectation of success, is necessary in order to fulfil the claimed invention, an isolated nucleotide molecule comprising a nucleotide sequence encoding CaEss1 having at least 70%homology fragments of SEQ.ID.NO 2 with at least one deletion in the peptide. What changes would have an adverse effect on the function of this peptide is not predictable. It is known in the art that deletions, or modifications of the amino acids of a protein alter the function of the protein. The amino acid

sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and still retain similar activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a single protein and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex (Bowie et al. Science, Vol. 247: 1990; p. 1306; p. 1308) and is well outside the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in protein and the result of such modifications is unpredictable based on the instant disclosure.

The specification does not support the broad scope of the claims which encompass a nucleic acid molecule encodes a fragment which can be predictably modified and which regions are critical; what variants, if any, can be made which retain the biological activity of the intact protein; and the specification provide essentially no guidance as to which of the essentially infinite possible choices is likely to be successful. Further, Houghten et al. (Vaccines, 1986, Edited by Fred Brown: Cold Spring Harbor Laboratory) teach that changes/modifications (addition, substitution, deletion or inversion) of one or more amino acids in a polypeptide will alter antigenic determinants and therefore affect antibody production (p. 21) as well as antibody binding. Houghten et al. also teach that "... combined effects of multiple changes in an

antigenic determinant could result in a loss of [immunological] protection." and "a protein having multiple antigenic sites, multiple point mutations, or accumulated point mutations at key residues could create a new antigen that is precipitously or progressively unrecognizable by any of the antibodies..." (p. 24). Houghten et al. teach that point mutations at one key antigen residue could eliminate the ability of an antibody to recognize this altered antigen (p. 24). It is not always possible to make the derivatives that retain immunodominant regions and immunological activity if the regions have been altered. The specification teaches that specific primer or probes are required to amplify the CaESS1 gene or its use a in diagnostic PCR for C.albicans (example 3, specification, pages 37-38). Therefore, any primer or probe would not work to amplify the CaESS1 gene or its use a in diagnostic PCR for C.albicans

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed nucleic acid molecule which encodes a fragment of a polypeptide (i.e., fragment with 70% homology), a primer or probe which specifically binds to a nucleic acid molecule comprising a nucleotide sequence encoding any and all variants of CaESS1, and a method for obtaining an isolated nucleic acid molecule encoding CaESS1 comprising performing a polymerase chain reaction on a sample to contain CaESS1 using any primer or probe which specifically hybridize thereto in a manner reasonably correlated with the scope of the claims broadly including any as presently claimed. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made in the protein renders activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acid's modification in such proteins. However, even if it were shown that some modifications could be tolerated in

the claimed peptides, for the reasons discussed the claims would still expectedly encompass a significant number of inoperative species which could not be distinguished without undue experimentation. See Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> a person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Springer et al 1996 (U.S.Patent 5,489,513).

Claims are directed to an isolated or purified nucleic acid molecule comprising a nucleotide sequence encoding CaEss1, or having at least 70% homology thereto and a primer or probe which specifically hybridizes to the nucleic acid molecule.

Springer et al 1996 (U.S.Patent 5,489,513) disclose isolation of nucleic acid from Candida (see column 5, lines 53 through column 6, lines 5). The isolated DNA inherently encodes CaEss1 since it is isolated from Candida. Further, the prior art discloses the detection of C.albicans by slot blot hybridization using polynucleotide probe 431.19 (see column 5, lines 33-51). Since the Office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

14. Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Accession Number AA182274 (January 6 1997)

Accession Number AA182274 (January 6 1997) discloses a probe comprising OW-221 (SEQ.ID.NO 6)

15. Claim 6 is rejected under 35 U.S.C. 102(b) as being anticipated by Accession Number Y 13120 (May 27 1997).

Accession Number Y 13120 (May 27 1997) discloses a probe comprising OW-216 (SEQ.ID.NO 3).

Status of Claims

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padma Baskar whose telephone number is (703) 308-8886. The examiner can normally be reached on Monday through Friday from 6:30 AM to 4 PM EST

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Padma Baskar Ph.D.

6/7/01

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600